BAUSCH & LOMB INCORPORATED TECHNOLAS 217z Zyoptix System for Personalized Vision Correction

WAVEFRONT-GUIDED LASER-ASSISTED IN SITU KERATOMILEUSIS (LASIK) PROFESSIONAL USE INFORMATION

- **For the reduction or elimination of myopia with sphere up to -7.00 D, cylinder up to -3.00 D and MRSE $\leq$ 7.50 D at the spectacle plane;**
- **in patients with documented evidence of a change in manifest refraction of less than or equal to ±0.50 diopters (in both cylinder and sphere components) for at least one year prior to the date of the pre-operative examination; and,**
- **in patients who are 21 years of age or older.**

RESTRICTED DEVICE: U.S. Federal Law restricts this device to sale, distribution, and use by or on the order of a physician or other licensed practitioner. U.S. Federal Law restricts this device to practitioners who have been trained in its calibration and operation and who have experience in the surgical management and treatment of refractive errors.

This document provides information concerning the intended clinical use of the Bausch & Lomb TECHNOLAS 217z Zyoptix System for Personalized Vision Correction. For complete information concerning system components, safety instructions, installation, maintenance, and troubleshooting, refer to the Bausch & Lomb TECHNOLAS 217z Excimer Laser System Operator's Manual.

Carefully read all instructions prior to use. Observe all contraindications, warnings, and precautions noted in these instructions. Failure to do so may result in patient and/or user complications.

Bausch & Lomb Incorporated
180 E. Via Verde Drive
San Dimas, CA 91773
Refractive Hotline:
(800) 496-7457
(800) 4xmr-hlp

TABLE OF CONTENTS

INDEX OF TABLES

SECTION 1
GENERAL WARNINGS

"WARNING:" - Identifies conditions or practices that could result in damage to equipment or other property, personal injury or loss of life.

"NOTE:" - Identifies conditions or practices warranting special attention.

WARNING: Specific training from Bausch & Lomb or an authorized representative of Bausch & Lomb is required before anyone is qualified to operate the Zyoptix™ Excimer Laser System. Read and understand this manual and the Zyoptix Excimer Laser System Operator's Manual prior to operating the system.

Refer to the Zyoptix Excimer Laser System *Operator's Manual* for additional warnings regarding use of the Zyoptix Excimer Laser System.

Restricted Device: Federal (U.S.) law restricts these devices to sale by or on the order of, a physician.

Carefully read all instructions prior to use. Observe all contraindications, warnings, and precautions.

Ventilation & Air-borne Contaminent
The treatment room must be adequately ventilated to provide air circulation. However, air contamination can cause attenuation of the ultraviolet laser radiation in the optical path, reducing the available power at the treatment site. It is recommended that a three stage 99.8% HEPA filtration system be used. Steps must be taken to keep the ambient air free of vapors from solvents or cleaning fluids, including floor wax and the adhesives used in new floor and wall coverings. Dust generating work and smoking are prohibited in the laser room. Use of air sterilization devices must be avoided. Disinfecting of the patient must not be carried out with volatile, organic hydrocarbons (alcohol). Storage of explosive or flammable substances in the treatment room is prohibited. Please refer to the Bausch & Lomb TECHNOLAS 217z Excimer Laser System User Guide, Section 4, Site Requirements and Installation.

Electromagnetic Compatibility
Radio interference or electromagnetic radiation can influence the function of the laser and/or other devices in the vicinity. The operator must remove possible interference sources. Persons wearing pacemakers should not be present in the treatment room when the laser is in operation. The use of mobile phones in the direct vicinity of the Bausch & Lomb TECHNOLAS 217z Excimer laser is not allowed as a negative influence cannot be ruled out. Please refer to the Bausch & Lomb TECHNOLAS 217z Excimer Laser System User Guide, Section 2, Safety considerations.

Gas Handling

The high-pressure gas cylinders should only be handled by service technicians professionally trained by Bausch & Lomb. Please refer to the Bausch & Lomb TECHNOLAS 217z Excimer Laser System (Zyoptix System) Operator's Manual, Section 2, Safety Considerations.

Skin and Eye Exposure

The Bausch & Lomb TECHNOLAS 217z Excimer Laser (Zyoptix 217z) contains a Class IV laser with an output at 193nm that is potentially hazardous to the skin and the surface layers of the cornea. For this reason, specific controls are required which prevent accidental exposure of laser energy to the eye and skin from both direct and reflected laser beams. In addition, precautions must be taken in the surgical area to prevent the hazards of fire and electrical injury. Please refer to the Bausch & Lomb TECHNOLAS 217z Excimer Laser System Operator's Manual, Section 2, Safety Considerations.

SECTION 2

DEVICE DESCRIPTION

2.1 WAVEFRONT ABERROMETER (Zywave)

The first step in performing Zyoptix® LASIK surgery is to perform a Wavefront examination on the patient using a Wavefront Detector (Zywave) compatible with the Zyoptix® Excimer Laser System. The only compatible Wavefront detector is the Bausch & Lomb ™ Zywave® Wavefront System. Essential features of Zywave are as follows:

PATIENT FIXATION AND FOGGING

The Zywave includes a fixation optical subsystem that provides the patient with a fixation point. In addition, the fixation subsystem includes adjustable optics to compensate for the patient's inherent refractive error. The optics are used to "fog" the eye, first clarifying the fixation target and then it optically adjusts beyond the patient's far point to minimize accommodation.

WAVEFRONT MEASUREMENT

The Zywave Wavefront sensor measures the Wavefront profile of the eye with a high degree of accuracy and characterizes the profile using Zernike polynomials up to and including the 5th Order

DATA EXPORT

The Zywave sensor has the ability to export the Wavefront examination data as an electronic file to floppy disk for transfer to the Zyoptix® system. The electronic file is structured in a specific format and contains essential patient information, and the detailed aberration data. In addition, the electronic file is encrypted in a manner that prohibits any data alteration or tampering prior to import into the Zylink Custom Treatment Planning Software.

2.2 MICROKERATOME

A microkeratome is used to achieve a partial thickness cut of the cornea, which creates a "flap" as part of the LASIK procedure. The microkeratome is a precision instrument used in performing lamellar corneal resections. This instrument cuts a corneal disc of pre-selected thickness and diameter. The system generally consists of a head, plates, ring, handle, wrenches, shaft, motor, hand-piece, disposable blades, and power supply with footswitches and power cords. The system is completed with the applanation lens set, tonometer, corneal storage jar, optical zone marker, spatula, stop attachment, and digital thickness gauge.

Microkeratome Used in the Clinical Trial:

The microkeratome used in the clinical trial was the Hansatome® (manufactured by Bausch & Lomb).

2.3 LASER SYSTEM with ACTIVE TRACKER

The specifications for the Bausch & Lomb TECHNOLAS Zyoptix 217z Laser are provided below.

Laser Type:	Argon Fluoride
Laser Wavelength:	193 nanometers
Laser Pulse Duration:	18 nanoseconds
Laser Head Repetition Rate:	50 Hz
Effective Corneal Repetition Rate:	12.5 Hz
Fluence (at the treatment area):	120 mJ/cm^2
Range of Ablation Diameter:	2 mm hard aperture: 2.0 to 2.05 mm
	2 mm soft aperture: 2.0 to 2.05 mm
	1 mm soft aperture: 1.0 to 1.05 mm
Active Eye Tracker	
- Tracking frequency	120 Hz

- Bausch & Lomb recommends use of the largest possible optic zone size based on the patient's wavefront data, while ensuring residual stromal thickness of 250 microns. The recommended optic zone should be selected from between 6.0 mm and 7.0 mm with a blend zone being held constant at 0.875 mm. A warning flag will appear when an optic zone <6.0 mm is selected. A warning flag will also appear in the event that the optic zone selected would result in residual stromal thickness of less than 250 microns. The ablation (treatment) zone is the sum of the optical zone selected plus the blend zone. This blend zone is smaller than that used in Planoscan Conventional LASIK, and results in a central ablation depth approximately 25% less than is required by the Planoscan Conventional LASIK procedure for treatment of myopia with sphere up to -7.00 D, cylinder up to –3.00 D and MRSE $\leq$ 7.50 D at the spectacle plane.

It should be noted that the optic zone cannot be selected to be larger than the patient's pupil size during the Wavefront measurement. Dilation to ensure a large optic zone is available to the surgeon during treatment planning is recommended.

FEATURES AND COMPONENTS OF THE ZYOPTIX 217Z LASER SYSTEM:

Laser Unit	The laser unit consists of the laser head (discharge system), which contains the optical resonator and a discharge chamber, which is filled with a premix of argon, fluorine, and a buffer of other noble gases.
Control Unit	The control unit contains the personal computer that uses a software algorithm to calculate the number and location of laser pulses required to achieve the desired correction.
Tower Unit	The tower unit provides the stable holding construction for the optical system of the Zyoptix 217z Laser. The tower unit contains the optical elements that condition the laser beam to the appropriate characteristics. The tower also contains the visualization optics (the operating microscope) and the positioning and fixation optics for properly locating and monitoring the progress of the ablation. There is a distance of 21 cm ("working distance") between the focusing point on the cornea and the laser arm.
Zyoptix Aperture Treatment Card	The Zyoptix Aperture Treatment Card (Aperture Card) softens the treatment laser beam edges to the truncated Gaussian formed beam through two different aperture diameters (1 mm and 2 mm).
Robotic Arm	The mechanical robotic arm provides the physical movement of the Aperture Card into the correct position of the laser's optical path.
Active Eye Tracker	The active eye tracker attaches to the laser to ensure the centration of the treatment on the cornea compensating for patient eye movement during treatment.
Operating Elements	The operating elements of the Bausch & Lomb Zyoptix Laser consist of two joysticks for movement of the patient bed in all axes and other operating elements and external connectors.
Bed Unit and Chair	The bed unit allows for accurate positioning of the patient during the surgical procedure while the operating chair allows the surgeon to adjust his/her position at the operating microscope.

2.4 TRACKING SYSTEM

The Zyoptix laser system includes a 120 Hz active eye-tracker. The eye tracking system enables the surgeon to select the treatment center of the ablation, and compensate for horizontal eye movements (x and Y directions) by the patient during surgery. The overall reaction time of the laser system to eye movement is 10.7 milliseconds, allowing the laser to

actively compensate for eye movements up to 24 mm per second. During treatment, if the eye-tracker detects movement greater than 24 mm per second during the treatment, the laser pulse will be paused momentarily until the rapid eye movements come back within the active range of the eye-tracker.

SECTION 3

INDICATIONS, CONTRAINDICATIONS, WARNINGS, PRECAUTIONS AND ADVERSE EVENTS

3.1. INDICATIONS FOR USE

The Bausch & Lomb TECHNOLAS 217z Zyoptix System for Personalized Vision Correction (Zyoptix System) is indicated for wavefront-guided laser in-situ keratomileusis (LASIK) treatments:

- for the reduction or elimination of myopia with sphere up to -7.00 D, cylinder up to –3.00 D and MRSE $\leq$ 7.50 D at the spectacle plane;
- in patients with documented evidence of a change in manifest refraction of less than or equal to ±0.50 diopters (in both cylinder and sphere components) for at least one year prior to the date of the pre-operative examination; and,
- in patients who are 21 years of age or older.

3.2. CONTRAINDICATIONS

LASIK surgery is contraindicated in:

- Patients with collagen vascular, autoimmune, or immunodeficiency diseases;
- Pregnant or nursing women;
- Patients with signs of keratoconus;
- Patients who are taking one or both of the following medications: isotretinoin (Accutane[1]), or amiodarone hydrochloride (Cordarone[2]).

3.3. WARNINGS

- The decision to perform LASIK surgery in patients with systemic disease likely to affect wound healing, such as connective tissue disease, diabetes, severe atopic disease or an immunocompromised status should be approached cautiously. The safety and effectiveness of the Zyoptix System has not been established in patients with these conditions.
- LASIK is not recommended in patients with a known history of *Herpes simplex* or *Herpes zoster.*
- LASIK is not recommended in patients who have:
  - insulin-dependent diabetes.
  - severe allergies.
  - significant dry eye that is unresponsive to treatment.

[1] Accutane is the registered trademark of Hoffman La Roche Inc.
[2] Cordarone is the registered trademark of Sanofi-Synthlabo

3.4. PRECAUTIONS

The safety and effectiveness of the Zyoptix System for LASIK have NOT been established:

- In patients with ocular disease, corneal abnormality, and previous corneal surgery or trauma to the intended ablation zone.
- In patients with prior history of refractive surgery (for example, RK, PRK, LASIK).
- In patients with corneal neovascularization within 1.0 mm of the ablation zone.
- In patients under 21 years of age.
- In patients taking hormone replacement therapy or antihistamines who may have delayed re-epithelialization of the cornea following surgery.
- In patients who are taking Sumatripin (Imitrex[3]) for migraine headaches.
- In patients with a history of glaucoma.
- For treatment of myopia greater than -7.00 D of sphere, astigmatism greater than -3.00 D, and MRSE greater than -7.50 D at the spectacle plane.
- In patients with a residual corneal thickness less than 250 microns at the completion of ablation (see the section on Operative Procedure).
- Over the long term (more than 6 months after surgery).
- For retreatment with Zyoptix LASIK.

Preoperative evaluation for dry eye should be performed. Patients should be advised of the potential for worsening of symptoms associated with dry eye syndrome post-LASIK surgery.

Pupil size should be evaluated under mesopic conditions, and patients with large mesopic pupils should be advised of the potential for negative effects on optical visual symptoms after surgery such as glare, halos, and difficulty with night driving.

Bausch & Lomb recommends selection of the largest optical zone between 6.0 and 7.0 mm, while ensuring residual stromal thickness of at least 250 microns. The optic zone cannot be selected to be larger than the patient's pupil size during the wavefront measurement. Bausch & Lomb recommends dilation to ensure a large optic zone is available to the surgeon during treatment planning.

LASIK is not recommended in patients whose preoperative corneal thickness would leave less than 250 microns of remaining non-ablated cornea following the laser treatment.

Lower proportions of eyes with uncorrected visual acuity of 20/32 or better and accuracy of MRSE within $\leq \pm$ 0.5 D of emmetropia may be anticipated following treatment of eyes with higher levels of preoperative MRSE (greater than or equal to –7.00 D MRSE).

[3] Imitrex is the trademark of Glaxo Group Ltd.

Significantly fewer eyes with smaller optical zone (less than 6.25 mm) achieved BCVA of 20/20 or better at 3 months and 20/16 or better at 6 months in the population of all treated eyes.

The physician's adjustment of defocus has not been studied, and its effects on the safety and effectiveness outcomes of this procedure are unknown. No adjustments were performed in the clinical trial. However, the permitted adjustment of the spherical term (defocus) is $\pm$ 0.75 diopters.

3.5. ADVERSE EVENTS AND COMPLICATIONS

Tables 1A and 1B present all the cumulative key safety, adverse events, and complications for all treated eyes reported in the study.

TABLE 1A

ADVERSE EVENTS SUMMARY
ALL TREATED EYES

	VISITS		
ALL REPORTED ADVERSE EVENTS	**1 MONTH**	**3 MONTHS**	**6 MONTHS**
Total Eyes Reported*	340	340	340
Not Reported**	0	0	0
Distribution of Scores	% (n)	% (n)	% (n)
Decrease in BSCVA of ≥ 2 lines not due to irregular astigmatism at ≥ 6 months	0.0% (0)	0.0% (0)	0.6% (2)
Epithelial defect	0.0% (0)	0.0% (0)	0.0% (0)
Keratome stopped	0.0% (0)	0.0% (0)	0.0% (0)
Lamellar keratitis	0.0% (0)	0.0% (0)	0.3% (1)
Secondary surgical intervention other than Excimer laser treatment	0.0% (0)	0.0% (0)	0.0% (0)

* Number of CRFs received with non-missing values at each visit.
** Number of CRFs received with missing values at each visit.

TABLE 1B

COMPLICATION SUMMARY
ALL TREATED EYES

	VISITS		
	1 MONTH	3 MONTHS	6 MONTHS
ALL REPORTED CONDITIONS	% (n)	% (n)	% (n)
Recurrent corneal erosion	0.0% (0)	0.0% (0)	0.3% (1)
Foreign body sensation	0.0% (0)	0.0% (0)	0.0% (0)
Pain	0.0% (0)	0.0% (0)	0.0% (0)
Size and shape of flap not as intended	0.0% (0)	0.0% (0)	0.0% (0)
Misplaced, misaligned, loose flap, or free cap with loss of ≤ 2 lines (≤ 10 letters) of BSCVA	0.0% (0)	0.3% (1)	0.0% (0)
Epithelium in the interface with loss of ≤ 2lines of BSCVA	0.3% (1)	0.0% (0)	0.0% (0)
Double vision	0.0% (0)	0.0% (0)	0.0% (0)
Ghost images	0.0% (0)	0.3% (1)	0.0% (0)
Peripheral corneal epithelial defect (on the flap)	0.0% (0)	0.0% (0)	0.0% (0)
Peripheral corneal epithelial defect (off the flap)	0.0% (0)	0.0% (0)	0.0% (0)
Peripheral corneal epithelial defect (across the junction)	0.0% (0)	0.0% (0)	0.0% (0)
Epithelial ingrowth	0.0% (0)	0.0% (0)	0.0% (0)
Other			
Allergy	0.3% (1)	0.3% (1)	0.0% (0)
Bowmans wrinkle	0.0% (0)	0.0% (0)	0.6% (2)
Chalazion	0.3% (1)	0.3% (1)	0.0% (0)
Conjunctivitis	0.3% (1)	0.3% (1)	0.6% (2)
Corneal abrasion	0.0% (0)	0.0% (0)	0.3% (1)
Debris in interface	5.3% (18)	2.4% (8)	1.2% (4)
Debris in interface & Browns wrinkle	0.0% (0)	0.0% (0)	0.6% (2)
Debris in interface & Episcleritis	0.3% (1)	0.0% (0)	0.0% (0)
Episcleritis	0.3% (1)	0.0% (0)	0.0% (0)
Inflammation, interface	0.3% (1)	0.0% (0)	0.0% (0)

SECTION 4

CLINICAL RESULTS

4.1. STUDY OBJECTIVES

A prospective, non-randomized, multicenter clinical study of 342 eyes was conducted to evaluate the safety and effectiveness of the Bausch & Lomb TECHNOLAS 217z Zyoptix System for Personalized Vision Correction

4.2. DATA ANALYSIS AND RESULTS

4.2.1. DEMOGRAPHIC AND BASELINE PARAMETERS

Demographic characteristics of the study population are presented in Table 2. Accountability for all treated eyes across the study visit schedule is presented in Table 3. The baseline attempted corrections for the study population are presented in Table 4.

TABLE 2

DEMOGRAPHICS – ALL TREATED EYES

		Total
Number of eyes*		342
Number of Enrolled Subjects		191
Age (yrs)	Mean	34.4
	SD	8.29
	Range	21-61
Gender	Male	46.1%
	Female	53.9%
Race	White	90.6%
	Black	1.1%
	Asian	5.2%
	Other	3.1%
Operative Eye	OD	49.7%
	OS	50.3%

*Two surgery aborted/not attempted eyes are included in the total number of eyes.

4.2.2 ACCOUNTABILITY

Accountability was excellent with no patients lost to follow-up, and no missed visits from 1 month forward. Two eyes were discontinued at the time of surgery due to intraoperative problems associated with the flap creation. No patients were retreated and no eyes were discontinued from the study due to visual symptoms.

TABLE 3

ACCOUNTABILITY
ALL TREATED EYES

	VISITS				
	DAY 1 % (n)	**DAY 7** % (n)	**1 MONTH** % (n)	**3 MONTHS** % (n)	**6 MONTHS** % (n)
Eyes Enrolled	342	342	342	342	342
Eyes Treated	340	340	340	340	340
Available for Efficacy Analysis†	100.0% (340)	99.4% (338)	100.0% (340)	100.0% (340)	100.0% (340)
Discontinued/Terminated*	0.6% (2)	0.6% (2)	0.6% (2)	0.6% (2)	0.6% (2)
Lost To Follow-Up	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)
Missed Visit**	0.0% (0)	0.6% (2)	0.0% (0)	0.0% (0)	0.0% (0)
Active (Not Yet Eligible For The Interval)	0.0%(0)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)

† The denominator for the percent is all eyes treated.

* One could not be treated due to a small flap and the patient was exited prior to the laser surgery. The other eye was also exited at time surgery due to creation of a flap that was too thin and epithelium on the cornea that was loose

** Missed visit: Eyes not examined at the scheduled visit, but were then seen at a subsequent visit

Preoperatively, the mean manifest sphere was -3.30 D and the mean cylinder was 0.68 D. The intended correction was the full manifest refraction spherical equivalent with the goal of achieving a plano refraction after the surgery.

TABLE 4

ATTEMPTED SPHERICAL (DEFOCUS) AND CYLINDRICAL (ASTIGMATISM) CORRECTION*
ALL TREATED EYES, N = 340

SPHERE	**CYLINDER** Mean = 0.71D; S.D. = 0.56D; Range = 0.02D – 3.12D					
Mean = 3.17D S.D. = 1.60D Range = 0.46D – 7.13D	**0.00-0.49D** % (n)	**0.50-0.99D** % (n)	**1.00-1.99D** % (n)	**2.00-2.99D** % (n)	**3.00-3.99D** % (n)	**Total** % (n)
0.00-0.99D	0.3% (1)	0.6% (2)	1.8% (6)	0.3% (1)	0.3% (1)	3.2% (11)
1.00-1.99D	11.5% (39)	7.6% (26)	4.7% (16)	2.1% (7)	0.0% (0)	25.9% (88)
2.00-2.99D	10.9% (37)	6.5% (22)	3.8% (13)	0.6% (2)	0.0% (0)	21.8% (74)
3.00-3.99D	7.4% (25)	7.9% (27)	3.2% (11)	0.6% (2)	0.0% (0)	19.1% (65)
4.00-4.99D	5.6% (19)	6.5% (22)	2.6% (9)	0.6% (2)	0.0% (0)	15.3% (52)
5.00-5.99D	4.4% (15)	2.9% (10)	0.3% (1)	0.3% (1)	0.0% (0)	7.9% (27)
6.00-6.99D	2.9% (10)	2.9% (10)	0.6% (2)	0.0% (0)	0.0% (0)	6.5% (22)
7.00-7.99D	0.3% (1)	0.0% (0)	0.0% (0)	0.0% (0)	0.0% (0)	0.3% (1)
Total	43.2% (147)	35.0% (119)	17.1% (58)	4.4% (15)	0.3% (1)	100.0% (340)

*Attempted correction was the complete refractive error generated using the Zywave device.

4.2.3. SAFETY AND EFFECTIVENESS RESULTS

The primary cohort consisted of 340 eyes including 117 eyes with less than -0.50D of astigmatism and 223 eyes with -0.50D to -3.5D of astigmatism based on manifest refraction.

4.2.3.1 Key Safety and Effectiveness Parameters by Treatment (All Eyes, Spherical Eyes, Spherocylindrical Eyes)

Tables 5A-C presents the summary of the key safety and effectiveness parameters for the 340 treated eyes, the 117 spherical eyes and the 223 spherocylindrical eyes, respectively, at all available postoperative visits.

Preoperatively none of the eyes had uncorrected visual acuity of 20/40 or better. Postoperative UCVA of 20/20 or better was reported in ≥ 90% of eyes from the point of stability (3 months) forward. Approximately 70% of eyes had UCVA of 20/16 or better.

TABLE 5A

SUMMARY OF KEY EFFICACY VARIABLES OVER TIME (N=340)

Efficacy Variables		1 Month	3 Months	6 Months
UCVA 20/16 or better	%	61.2%	69.4%	70.3%
	(n/N)	208/340	236/340	239/340
	CI	54.8, 67.6	63.4, 75.4	64.4, 76.2
UCVA 20/20 or better	%	85.6%	90.3%	91.5%
	(n/N)	291/340	307/340	311/340
	CI	81.3, 89.9	86.7, 93.9	88.0, 95.0
UCVA 20/25 or better	%	94.4%	95.0%	95.3%
	(n/N)	321/340	323/340	324/340
	CI	91.4, 97.4	92.0, 98.0	92.7, 97.9
UCVA 20/32 or better	%	98.2%	98.2%	98.5%
	(n/N)	334/340	334/340	335/340
	CI	96.6, 99.8	96.6, 99.8	97.3, 99.8
UCVA 20/40 or better	%	99.4%	99.1%	99.4%
	(n/N)	338/340	337/340	338/340
	CI	97.9, 99.9	97.8, 100	97.9, 99.9
MRSE ≤ ±0.50D of intended	%	73.8%	77.6%	75.9%
	(n/N)	251/340	264/340	258/340
	CI	68.3, 79.3	72.4, 82.9	70.2, 81.6
MRSE≤ ±1.00D of intended	%	93.8%	93.8%	93.8%
	(n/N)	319/340	319/340	319/340
	CI	90.8, 96.8	91.1, 96.6	91.1, 96.6
Safety Variables		**1 Month**	**3 Months**	**6 Months**
Loss of >2 Lines BSCVA	%	0.6%	0.0%	0.0%
	(n/N)	2/340	0/340	0/340
	CI	0.1, 2.1	0.0, 1.1	0.0, 1.1
Loss of ≥ 2 Lines BSCVA	%	1.5%	1.2%	0.6%
	(n/N)	5/340	4/340	2/340
	CI	0.2, 2.7	0, 2.6	0, 2.1
BSCVA worse than 20/40	%	0.3%	0	0
	(n/N)	1/340	0/340	0/340
	CI	0.0, 1.6	0, 1.1	0. 1, 1.1
BSCVA worse than 20/25 if 20/20 or better preoperatively	%	0.6%	0.3%	0
	(n/N)	2/335	1/335	0/335
	CI	0.1, 2.1	0. 1.7	0, 1.1

BSCVA = Best spectacle corrected visual acuity
MRSE = Manifest refraction spherical equivalent
CI = 95% Confidence interval for percentage
UCVA = Uncorrected visual acuity

TABLE 5B

SUMMARY OF KEY EFFICACY VARIABLES OVER TIME SPHERICAL EYES (N=117)

Efficacy Variables		1 Month	3 Months	6 Months
UCVA 20/16 or better	%	65.8%	73.5%	74.4%
	(n/N)	77/117	86/117	87/117
	CI	55.8, 75.8	63.4, 82.7	65.3, 83.5
UCVA 20/20 or better	%	92.3%	90.6%	94.0%
	(n/N)	108/117	106/117	110/117
	CI	86.9, 97.7	84.8, 96.4	89.1, 98.9
UCVA 20/25 or better	%	97.4%	96.6%	95.7%
	(n/N)	114/117	113/117	112/117
	CI	92.7, 99.5	92.5, 100	91.3, 100
UCVA 20/32 or better	%	98.3%	98.3%	98.3%
	(n/N)	115/117	115/117	115/117
	CI	94.0, 99.8	94.0, 99.8	94.0, 99.8
UCVA 20/40 or better	% (n/N)	100.0%	100.0%	100.0%
	CI	117/117	117/117	117/117
		96.9, 100	96.9, 100	96.9, 100
MRSE ≤ ±0.50 D of intended	%	81.2%	84.6%	84.6%
	(n/N)	95/117	99/117	99/117
	CI	73.2, 89.2	77.4, 91.9	77.4, 91.9
MRSE ≤ ±1.00 D of intended	%	94.0%	94.9%	96.6%
	(n/N)	110/117	111/117	113/117
	CI	89.1, 98.9	89.2, 98.1	91.5, 99.1
Safety Variables		**1 Month**	**3 Months**	**6 Months**
Loss of >2 Lines BSCVA	%	0%	0%	0%
	(n/N)	0/117	0/117	0/117
	CI	0.0, 3.1	0.0, 3.1	0.0, 3.1
Loss of ≥ 2 Lines BSCVA	%	0.0%	0.9%	0.9%
	(n/N)	0/117	1/117	1/117
	CI	0.0, 3.1	0.0, 4.7	0.0, 4.7
BSCVA worse than 20/40	%	0%	0%	0%
	(n/N)	0/117	0/117	0/117
	CI	0.0, 3.1	0.0, 3.1	0.0, 3.1
Increase >2D cylinder magnitude	%	0.0%	0.0%	0.0%
	(n/N)	0	0	0
BSCVA worse than 20/25	%	0%	0%	0%
if 20/20 or better preoperatively	(n/N)	0/115	0/115	0/115
	CI	0.0, 3.2	0.0, 3.2	0.0, 3.2

BSCVA = Best spectacle corrected visual acuity
CI = 95% Confidence interval for percentage
MRSE = Manifest refraction spherical equivalent
UCVA = Uncorrected visual acuity

TABLE 5C

SUMMARY OF KEY EFFICACY VARIABLES OVER TIME SPHEROCYLINDRICAL EYES (N=223)

Efficacy Variables		1 Month	3 Months	6 Months
UCVA 20/16 or better	% (n/N)	58.7%	67.3%	68.2%
	CI	131/223	150/223	152/223
		50.9, 66.6	59.8, 74.7	60.9, 75.4
UCVA 20/20 or better	%	82.1%	90.1%	90.1%
	(n/N)	183/223	201/223	201/223
	CI	76.3, 87.9	85.6, 94.6	85.6, 94.6
UCVA 20/25 or better	%	92.8%	94.2%	95.1%
	(n/N)	207/223	210/223	212/223
	CI	88.6, 97.1	90.3, 98.1	92.0, 98.1
UCVA 20/32 or better	%	98.2%	98.3%	98.7%
	(n/N)	219/223	219/223	220/223
	CI	96.1, 100	96.1, 100	97.2, 100
UCVA 20/40 or better	%	99.1%	99.1%	99.1%
	(n/N)	221/223	220/223	221/223
	CI	96.8, 99.9	96.7, 100	96.8, 99.9
MRSE ≤ ±0.50 D of intended	%	70.0%	74.0%	71.3
	(n/N)	156/221	165/223	159/223
	CI	63.0, 77.0	67.5, 80.5	64.2, 78.4
MRSE ≤ ±1.00 D of intended	%	93.7%	93.3%	92.4%
	(n/N)	209/223	208/223	206/223
	CI	90.2, 97.3	89.8, 96.7	88.2, 96.5
Safety Variables		**1 Month**	**3 Months**	**6 Months**
Loss of >2 Lines BSCVA	%	0.9%	0.0%	0.0%
	(n/N)	2/223	0/223	0/223
	CI	0.1, 3.2	0.0, 1.6	0.0, 1.6
Loss of ≥ 2 Lines BSCVA	%	2.2%	1.3%	0.4%
	(n/N)	5/223	3/223	1/223
	CI	0.3, 4.2	0.0, 3.3	0.0, 2.5
BSCVA worse than 20/40	%	0.4%	0.0%	0.0%
	(n/N)	1/223	0/223	0/223
	CI	0.0, 2.5	0.0, 1.6	0.0, 1.6
BSCVA worse than 20/25 if 20/20 or better preoperatively	%	0.9%	0.5%	0.0%
	(n/N)	2/220	1/220	0/220
	CI	0.1, 3.2	0.0, 2.5	0.0, 1.7

BSCVA = Best spectacle corrected visual acuity
CI = 95% Confidence interval for percentage
MRSE = Manifest refraction spherical equivalent
UCVA = Uncorrected visual acuity

4.2.3.2 Key Effectiveness Parameters by Preoperative MRSE

Tables 6A and 6B present the results for key safety and effectiveness for all treated eyes at 3 months and at 6 months, respectively, stratified by preoperative MRSE.

Lower proportions of eyes with uncorrected visual acuity of 20/32 or better and accuracy of MRSE within ≤ ± 0.5 D of emmetropia may be anticipated following treatment of eyes with higher levels of preoperative MRSE (greater than or equal to –7.00 D MRSE).

TABLE 6A

SUMMARY OF KEY EFFICACY VARIABLES AT 3 MONTHS STRATIFIED BY PREOPERATIVE MANIFEST REFRACTIVE SPHERICAL EQUIVALENT ALL TREATED EYES

	PREOPERATIVE MANIFEST REFRACTIVE SPHERICAL EQUIVALENT						
KEY EFFICACY VARIABLES	**1.00–1.99 D** % (n)	**2.00–2.99 D** % (n)	**3.00–3.99 D** % (n)	**4.00–4.99 D** % (n)	**5.00–5.99 D** % (n)	**6.00–6.99 D** % (n)	**7.00-7.99D** % (n)
Total Eyes Reported*	41	86	82	57	39	27	8
UCVA 20/16 or Better	70.7 % (29)	77.9% (67)	67.1% (55)	59.6% (34)	64.1% (25)	81.5% (22)	50.0% (4)
UCVA 20/20 or Better	95.1 % (39)	91.9% (79)	91.5% (75)	87.7% (50)	84.6% (33)	92.6% (25)	75.0% (6)
UCVA 20/25 or Better	100.0 % (41)	97.7% (84)	96.3% (79)	93.0% (53)	89.7% (35)	92.6% (25)	75.0% (6)
UCVA 20/32 or Better	100.0 % (41)	100.0% (86)	98.8% (81)	100.0% (57)	97.4% (38)	92.6% (25)	75.0% (6)
UCVA 20/40 or Better	100.0 % (41)	100.0%(86)	98.8% (81)	100.0% (57)	100.0% (39)	92.6% (25)	100.0% (8)
MRSE ≤ ± 0.50 D	90.2 % (37)	84.9% (73)	76.8% (63)	71.9% (41)	74.4% (29)	74.1% (20)	12.5% (1)
MRSE ≤ ± 1.00 D	97.6 % (40)	96.5% (93)	92.7% (76)	94.7% (54)	92.3% (36)	85.2% (23)	87.5% (7)

* Number of CRFs received with non-missing values.

TABLE 6B

SUMMARY OF KEY EFFICACY VARIABLES AT 6 MONTHS STRATIFIED BY PREOPERATIVE MANIFEST REFRACTIVE SPHERICAL EQUIVALENT ALL TREATED EYES

	PREOPERATIVE MANIFEST REFRACTIVE SPHERICAL EQUIVALENT						
KEY EFFICACY VARIABLES	**1.00–1.99 D** % (n)	**2.00–2.99 D** % (n)	**3.00–3.99 D** % (n)	**4.00–4.99 D** % (n)	**5.00–5.99 D** % (n)	**6.00–6.99 D** % (n)	**7.00-7.99D** % (n)
Total Eyes Reported*	41	86	82	57	39	27	8
UCVA 20/16 or Better	73.2% (30)	77.9% (67)	70.7% (58)	66.7% (38)	61.5% (24)	66.7% (18)	50.0% (4)
UCVA 20/20 or Better	97.6% (40)	95.3% (82)	92.7% (76)	91.2% (52)	84.6% (33)	81.5% (22)	75.0% (6)
UCVA 20/25 or Better	100.0% (41)	97.7% (84)	95.1% (78)	96.5% (55)	89.7% (35)	92.6% (25)	75.0% (6)
UCVA 20/32 or Better	100.0% (41)	100.0% (86)	97.6% (80)	100.0% (57)	97.4% (38)	96.3% (26)	87.5% (7)
UCVA 20/40 or Better	100.0% (41)	100.0% (86)	98.8% (81)	100.0% (57)	100.0% (39)	96.3% (26)	100.0% (8)
MRSE ≤ ± 0.50 D	95.1% (39)	82.6% (71)	72.0% (59)	75.4% (43)	69.2% (27)	66.7% (18)	12.5% (1)
MRSE ≤ ± 1.00 D	100.0% (41)	97.7% (84)	92.7% (76)	96.5% (55)	89.7% (35)	81.5% (22)	75.0% (6)

* Number of CRFs received with non-missing values.

4.2.3.3 Influence of Optic Zone Size Selection on Key Effectiveness Parameters

In the Zyoptix clinical trial, the investigators had the opportunity to select the optic zone size to use, with an effort made to keep the size at 6.0 mm or larger. There were only 3 eyes in the study with an optical zone of less than 6.0mm, each of which occurred based on the medical judgment of the surgeon at the time of the treatment. All three eyes had an optic zone of 5.8 mm and had UCVA of 20/20 or better at the 6-month postoperative evaluation.

An evaluation of the clinical results as a function of the optic zone size indicates that the results favor use of the largest possible optic zone size, while ensuring residual stromal thickness of 250 microns. The optic zone can be selected between the 6.0 mm and 7.0 mm with a blend zone being held constant at 0.875 mm. The blend zone is smaller than that used in Planoscan Conventional LASIK, resulting in a central ablation depth that is approximately 25% less than the ablation depth required by the Planoscan Conventional LASIK procedure for the reduction or elimination of myopia with sphere up to -7.00 D, cylinder up to –3.00 D and MRSE $\leq$ 7.50 D at the spectacle plane;

The effectiveness results by optic zone size for all study eyes are found in Table 7 below. No statistically significant differences among the optic zone groups were found on the parameters of MRSE within 0.5 and 1.0 diopters of emmetropia, or on achievement of UCVA of 20/16 or better, and 20/25 or better. Significant differences, favoring larger optic zones were found on the parameters of UCVA 20/20 or better, 20/32 or better and 20/40 or better.

Extensive analyses were performed to evaluate the effect of both treatment (i.e., sphere only or spherocylindrical corrections) and of optical zone size on safety and efficacy outcomes following treatment with the Zyoptix System. At both 3 months and 6 months, in the cohort of all treated eyes and in spherocylindrical eyes, smaller optical zones (less than 6.25 mm) were associated with lower proportions of eyes with UCVA of 20/20, 20/25, 20/32 and 20/40. No statistically significant differences in UCVA were observed across the optical zones for sphere only eyes, however, at 6 months, the proportion of spherical eyes with MRSE within 0.50 D of emmetropia was significantly lower for eyes treated with smaller optical zone (less than 6.25 mm). Notwithstanding these differences, all efficacy targets established in FDA guidance for clinical trials of excimer lasers were achieved or exceeded for all three cohorts (all treated eyes, sphere only eyes, spherocylindrical eyes) and for all optical zone sizes.

With regard to stratification of key safety variables by optical zone, because of the small number of adverse events and complications in the study population, stratification of these data by optical zone would not provide any statistically meaningful information. For this reason, this analysis was limited to stratification of BCVA by treatment and by optical zone. Significantly fewer eyes with smaller optical zone (less than 6.25 mm) achieved BCVA of 20/20 or better at 3 months and 20/16 or better at 6 months in the population of all treated eyes. In spherocylindrical eyes, at 3 and 6 months, the proportion of eyes with BCVA of 20/16 or better was smaller for eyes with smaller optical zone (less than 6.25 mm). No differences were observed across the three optical zone groups for the sphere only eyes, and it should be noted that all eyes (100%) achieved

BCVA of 20/25 or better at 6 months, and nearly all eyes (95% or greater) achieved BCVA of 20/20 or better at 6 months.

Bausch & Lomb recommends selection of the largest optical zone between 6.0 and 7.0 mm, while ensuring residual stromal thickness of at least 250 microns. A warning flag will appear when an optic zone <6.0 mm is selected. Optic zone cannot be selected to be larger than the patient's pupil size during the wavefront measurement. Dilation to ensure that a large optic zone is available to the surgeon for treatment planning is recommended.

Please refer to Section 4.2.9.3 for information on the effect of optical zone on patients symptoms, and to Section 4.2.11.3 for information on change from baseline in wavefront aberrations as a function of optic zone.

TABLE 7

SUMMARY OF KEY EFFICACY VARIABLES AT 6 MONTHS STRATIFIED BY OPTICAL ZONE SIZE ALL TREATED EYES

	OPTICAL ZONE SIZE (mm)			
KEY EFFICACY VARIABLES	**5.75-6.24** % (n)	**6.25-6.74** % (n)	**6.75-7.24** % (n)	**p-value**
Total Eyes Reported*	73	246	20	
UCVA 20/16 or Better	60.3% (44)	73.6% (181)	65.0% (13)	0.0802
UCVA 20/20 or Better	83.6% (61)	93.5% (230)	95.0% (19)	0.0249
UCVA 20/25 or Better	90.4% (66)	96.7% (238)	95.0% (19)	0.0798
UCVA 20/32 or Better	94.5%(69)	99.6% (245)	100.0% (20)	0.0054
UCVA 20/40 or Better	97.3% (71)	100.0% (246)	100.0% (20)	0.0237
MRSE ≤ ± 0.5 D	67.1% (49)	78.9% (194)	70.0% (14)	0.1004
MRSE ≤ ± 1.0 D	91.8% (67)	94.7% (233)	90.0% (18)	0.5152

* Number of CRFs received with non-missing values.

** p-value for comparison of optical zone strata (Cochran-Mantel-Haenszel test, stratified by primary and fellow eye designations).

4.2.4 MANIFEST REFRACTION OVER TIME

Table 8 provides the mean refraction spherical equivalent over time. The postoperative mean refraction for the population is consistent over the term of the study.

TABLE 8

MANIFEST REFRACTION SPHERICAL EQUIVALENT OVER TIME

Mean ± Standard Deviation	**Preop**	**1 Month**	**3 Months**	**6 Months**
All Eyes N=340	-3.66 ± 1.53	0.15 ± 0.54	0.15 ± 0.50	0.15 ± 0.51
Spherical Eyes N=117	-3.41 ± 1.60	0.06 ± 0.53	0.07 ± 0.47	0.02 ± 0.48
Spherocylindrical Eyes N =223*	-3.80 ± 1.48	0.20 ± 0.54	0.20 ± 0.51	0.22 ± 0.51

* Preop value based on N=340 for all eyes and N=-225 for spherocylindrical eyes

4.2.5 STABILITY OF THE MANIFEST REFRACTION

Results for stability of the manifest refraction as determined by the manifest spherical equivalent refraction are presented in Tables 9A to 9C for those eyes that had data at all scheduled follow-up visits during the study (the "consistent cohort").

TABLE 9A

STABILITY OF MANIFEST REFRACTION SPHERICAL EQUIVALENT FOR ALL TREATED EYES

Change in Spherical Equivalent Between	**1 and 3 Months**	**3 and 6 Months**
≤ 0.50 Diopter (%, n/N)	86.8% (295/340)	90.9%, (309/340)
≤ 1.00 Diopter (%, n/N)	96.2% (327/340)	98.5% (335/340)
Mean Difference ± Standard Deviation	0.00 ± 0.41	0.00 ± 0.35
95% Confidence Interval	-0.054, 0.054	-0.046, 0.046

TABLE 9B

STABILITY OF MANIFEST REFRACTION SPHERICAL EQUIVALENT FOR SPHERICAL TREATED EYES

Change in Spherical Equivalent Between	1 and 3 Months	3 and 6 Months
≤ 0.50 Diopter (%, n/N)	84.6% (99/117)	94.9% (11/117)
≤ 1.00 Diopter (%, n/N)	95.7% (112/117)	98.3% (115/117)
Mean Difference ± Standard Deviation	0.00 ± 0.44	-0.04 ± 0.32
95% Confidence Interval	-0.083, 0.085	-0.106, 0.023

TABLE 9C

STABILITY OF MANIFEST REFRACTION SPHERICAL EQUIVALENT FOR ASTIGMATIC TREATED EYES

Change in Spherical Equivalent Between	1 and 3 Months	3 and 6 Months
≤ 0.50 Diopter (%, n/N)	87.9% (196/223)	88.8% (198/223)
≤ 1.00 Diopter (%, n/N)	96.4% (215/223)	98.7% (220/223)
Mean Difference ± Standard Deviation	0.00 ± 0.39	0.02 ± 0.37
95% Confidence Interval	-0.060, 0.060	-0.035, 0.080

4.2.6. Cylinder Correction/Vector Analysis

Table 10 presents the results of the mean percent reduction of astigmatism for spherocylindrical eyes, stratified by preoperative cylinder and the correction ratio of achieved vector versus intended vector magnitude.

TABLE 10
CYLINDER CORRECTION EFFICACY AT 3 MONTHS
STRATIFIED BY PREOPERATIVE CYLINDER
SPHEROCYLINDRICAL EYES

Preoperative Cylinder	N	Mean Percent Reduction Of Absolute Cylinder (Non-Vector)	Correction Ratio Achieved VS. Intended Vector Magnitude Ratio (SIRC/IRC)
All	223	64.0% ± 43.0%	1.00 ± 0.40
0.50 to <1.00 D	134	58.8% ± 51.0%	1.03 ± 0.43
1.00 to < 2.00 D	69	70.1% ± 26.3%	0.98 ± 0.27
2.00 to < 3.00 D	18	78.0% ± 19.3%	1.00 ± 0.26
3.00 to < 4.00 D	2	76.9% ± 0.0%	0.89 ± 0.17

4.2.7. Correlation to Preoperative Best Corrected Visual Acuity

As shown in Table 11, best-corrected visual acuity was unchanged or improved in 90.9% of eyes at 1 months, in 93.0% of eyes at 3 months, and in 94.1% of eyes at 6 months. No eyes lost more than 2 lines, and two eyes lost 2 lines. One of these eyes was 20/12.5 preop and 20/20 at 6 months; the other was 20/16 preop and 20/25 at 6 months.

TABLE 11

CHANGE IN BEST SPECTACLE CORRECTED VISUAL ACUITY
FOR ALL EYES

	1 Month	3 Months	6 Months
	% (n/N)	% (n/N)	% (n/N)
	N=340	N=340	N=340
Decrease >2 Lines	0.6% (2)	0.0% (0)	0.0% (0)
Decrease 2 Lines	0.9% (3)	1.2 % (4)	0.6% (2)
Decrease 1 Line	7.6% (26)	5.9% (20)	5.3% (18)
No change	37.6% (128)	38.8% (132)	33.8% (115)
Increase 1 Line	36.2% (123)	35.6% (121)	41.5% (141)
Increase 2 Lines	15.3% (52)	17.3% (59)	17.3% (59)
Increase >2 Lines	1.8% (6)	1.2% (4)	1.5% (5)

Table 12 shows that at 3 months after surgery 77.3% of the patients and at 6 months after the surgery 78% of the patients saw as well ***without*** glasses after Zyoptix surgery as *with* glasses before surgery.

TABLE 11

VISUAL ACUITY *WITHOUT* GLASSES AFTER SURGERY COMPARED TO *WITH* GLASSES BEFORE SURGERY (N=340)

Time after Surgery	3 Months % (n)	6 Months % (n)
Percent of eyes with UCVA ≥2 lines better than preoperative BCVA	13.5% (46)	14.1% (48)
Percent of eyes with UCVA 1 line better than preoperative BCVA	25.6% (87)	27.9% (95)
Percent of eyes with UCVA equal to preoperative BCVA	38.2% (130)	36.2% (123)
Percent of eyes with UCVA 1 line worse than preoperative BCVA	15.3% (52)	14.7% (50)
Percent of eyes with UCVA ≥2 lines worse than preoperative BCVA	7.4% (25)	7.1% (24)

4.2.8. CHANGE IN CONTRAST SENSITIVITY AFTER SURGERY

A contrast sensitivity study was conducted to assess the effects of Zyoptix® myopic LASIK surgery to help determine how well patients see in conditions such as very dim light, rain, snow, and fog. The method used was Vision Sciences CST 1500 with FACT charts. Under mesopic lighting the conditions were controlled within the CST 1500 unit itself.

Table 13 shows the change in contrast sensitivity measured under photopic and mesopic lighting conditions after Zyoptix surgery compared to preoperative levels. Nearly all patients (97.9%) had no change or improvements in mesopic testing; 22.7% improved and only 2.1% were worse. Similarly, 96.5% of patients had no change or improvements in photopic testing; 24.4% improved and only 3.5% were worse.

TABLE 13
PROPORTION OF THE POPULATION WITH CHANGE OF >2 LEVELS (> 0.3 LOG) ON CSV-1500 AT 2 OR MORE SPATIAL FREQUENCIES FOR SPHERICAL MYOPIC EYES AT 6 MONTHS

	Photopic Conditions		
Change > 0.3 (log unit)	**Decrease**	**No Change**	**Increase**
% (n/N)	3.5%	72.1%	24.4%
	Mesopic Conditions		
Change > 0.3 (log unit)	**Decrease**	**No Change**	**Increase**
% (n/N)	2.1%	75.2%	22.7%

4.2.9. PATIENT SYMPTOMS AND SATISFACTION

4.2.9.1 Change in Clinically Significant Symptoms

The change from preoperative incidence of clinically significant symptoms (moderate, marked and severe) is found in Table 14A at the 3 and 6 month intervals. At 6 months significant differences in the incidence of clinically significant symptoms favoring improvement (reduced symptoms) occurred for the vision associated parameters of difficulties with night driving, variation of vision under bright light, and light sensitivity, and for the comfort associated parameters of headaches, pain, redness, and blurry vision. Significant differences in worsening symptoms were reported for the parameters of vision-associated parameters of double and fluctuating vision.

TABLE 14A

INCIDENCE OF CLINICALLY SIGNIFICANT* SYMPTOMS PREOPERATIVE AND POSTOPERATIVE

Patient Symptom	N**	Occurrence (%)+		P-value	N**	Occurrence (%)+		P-value
		Preop	3 Months	++		Preop	6 Months	++
Light Sensitivity	340	18.5%	4.7%	<.0001	340	18.5%	2.6%	<.0001
Headache	340	9.7%	5.3%	0.0090	340	9.7%	4.1%	0.0004
Pain	340	2.4%	0.3%	0.0196	340	2.4%	0.0%	0.0047
Redness	340	3.5%	3.2%	0.8084	340	3.5%	1.5%	0.0896
Dryness	340	7.9%	16.5%	0.0003	340	7.9%	5.9%	0.2623
Excessive Tearing	340	2.4%	0.0%	0.0047	340	2.4%	0.6%	0.0578
Burning	340	2.1%	2.1%	1.0000	340	2.1%	0.6%	0.0956
Gritty Feeling	340	0.9%	1.5%	0.4795	340	0.9%	0.3%	0.3173
Glare	340	4.4%	5.0%	0.7150	340	4.4%	3.5%	0.5637
Halos	340	2.6%	5.0%	0.1025	340	2.6%	3.8%	0.3938
Blurring of Vision	340	11.5%	7.4%	0.0390	340	11.5%	7.1%	0.0287
Double Vision	340	0.3%	0.9%	0.3173	340	0.3%	2.4%	0.0196
Ghost Images	340	0.9%	1.5%	0.3173	339	0.9%	1.8%	0.1797
Fluctuation of Vision	336	0.9%	7.4%	<.0001	335	0.9%	5.4%	0.0011
Variation in Vision:								
In Bright Light	340	7.4%	0.6%	0.0025	339	7.4%	1.2%	<.0001
In Normal Light	340	1.5%	2.1%	0.5637	339	1.5%	2.9%	0.1967
In Dim Light	340	11.8%	6.5%	0.0162	339	11.5%	10.6%	0.6858
Night Driving Difficulty	340	18.5%	8.8%	<.0001	340	18.5%	7.1%	<.0001
Other+++	325	0.6%	2.2%	0.0956	324	0.6%	3.7%	0.0075

* Absent/Mild scores were considered clinically insignificant. Moderate/Marked/Severe scores were considered clinically significant.
** Number of eyes reporting scores at both visits. This number was used as the denominator for calculating percentages. Rates for eyes reporting data at both visits.
\+ Minor variations from sums are due to rounding.
++ McNemar's test comparing occurrence rates at preop and 3 months; and at preop and 6 months.
+++Other symptoms included difficulty reading, eye strain, itchiness, starburst, floaters, and headache.

4.2.9.2 Change in Symptoms from Baseline at 3 and 6 months

Patients were asked to rate the following symptoms at 3 and 6 months compared to before Zyoptix LASIK surgery for the correction of spherical myopia. As shown in Table 14B, patients rated symptoms as significantly better, better, no change, worse, or significantly worse than preoperative. At 6 months, significant differences favoring improvement (reduced symptoms) compared to worsening were reported for the parameters of light sensitivity, headaches, pain, redness, excessive tearing, burning, variation of vision under bright light and dim light, and difficulties with night driving. Significant differences in worsening symptoms were reported for the parameters of dryness, and fluctuating vision.

TABLE 14B. COMPARISON OF SYMPTOMS BEFORE AND AFTER SURGERY

Symptom	Significantly Better	Better	No Change	Worse	Significantly Worse
3 Months (N=340)					
Light Sensitivity	8.2%	26.5%	54.4%	8.8%	2.1%
Headache	5.0%	19.4%	68.5%	5.3%	1.8%
Pain	2.4%	3.8%	92.1%	1.5%	0.3%
Redness	1.2%	17.4%	71.8%	7.9%	1.8%
Dryness	1.2%	11.8%	46.8%	30.6%	9.7%
Excessive Tearing	2.1%	8.8%	87.6%	1.5%	0.0%
Burning	0.3%	11.2%	75.6%	12.4%	0.6%
Gritty Feeling	0.6%	7.4%	81.5%	9.7%	0.9%
Glare	2.9%	12.9%	64.4%	16.5%	3.2%
Halos	1.5%	7.9%	69.1%	17.6%	3.8%
Blurring of Vision	7.9%	12.6%	60.3%	15.9%	3.2%
Double Vision	0.3%	1.2%	95.3%	2.4%	0.9%
Ghost Images**	0.3%	3.5%	91.8%	3.5%	0.9%
Fluctuation of Vision*	0.0%	7.4%	62.5%	24.1%	6.0%
Variation in Vision:					
In Bright Light	3.8%	17.9%	65.9%	10.9%	1.5%
In Normal Light	0.9%	8.2%	78.8%	10.6%	1.5%
In Dim Light	5.9%	18.2%	57.9%	15.6%	2.4%
Night Driving Difficulty	10.0%	24.4%	52.6%	12.1%	0.9%
6 Months (N=340)					
Light Sensitivity	9.4%	27.4%	55.6%	7.1%	0.6%
Headache	5.9%	19.4%	69.4%	4.1%	1.2%
Pain	2.4%	3.8%	91.8%	2.1%	0.0%
Redness	1.8%	21.5%	65.9%	9.7%	1.2%
Dryness	2.9%	16.8%	49.1%	28.8%	2.4%
Excessive Tearing	2.1%	10.0%	84.1%	3.2%	0.6%
Burning	1.2%	13.2%	77.6%	7.6%	0.3%
Gritty Feeling	0.6%	7.9%	85.3%	6.2%	0.0%
Glare	3.5%	17.4%	63.8%	12.1%	3.2%
Halos	1.8%	11.8%	72.1%	11.8%	2.6%
Blurring of Vision	8.5%	13.8%	59.1%	14.7%	3.8%
Double Vision	0.3%	1.2%	95.3%	0.9%	2.4%
Ghost Images**	0.3%	4.1%	91.2%	3.5%	0.9%
Fluctuation of Vision*	0.0%	7.5%	68.4%	20.0%	4.2%
Variation in Vision*:**					
In Bright Light	3.8%	20.1%	65.5%	10.3%	0.3%
In Normal Light	0.9%	8.6%	79.4%	8.8%	2.4%
In Dim Light	5.0%	20.4%	57.2%	14.7%	2.7%
Night Driving Difficulty	11.2%	29.1%	49.4%	9.1%	1.2%

* Fluctuation in Vision only reported on for n=336 eyes at 3 months and 335 eyes at 6 months

** Ghost images was reported on for n=339 eyes at 6 months

*** Variation in Vision was reported on for only n=339 eyes at 6 months

4.2.9.3 Influence Of Optic Zone Size On Patient Symptoms

Patient symptoms at 6 months were also analyzed by range of optic zone size used in the treatment. These results are provided in Table 15 below.

At 6 months, significant improvement in night driving difficulty was reported for all optic zones.

In addition, significant improvements (reduced symptoms) occurred for the parameters of headache, and redness for the optic zones of 5.75 to 6.24 mm and 6.25 to 6.74 mm. Significant improvements also occurred for the parameter of light sensitivity for both the 6.25-6.74 mm and the 6.75-7.24 mm optic zones. Additional significant improvements occurred for the parameters of pain, excessive tearing, burning, gritty feeling, and variations in vision under bright light for the 6.25-6.74 mm zone and in the parameters of blurry vision for the 6.75-7.24 mm optic zone.

Significant worsening occurred on the parameters of dryness for the smallest and largest zone. In addition significantly worse fluctuation in vision occurred for the smallest and mid-size optic zones. And there was significant worsening of double vision for the smallest optic zone.

As the optic zone size increased, there was a trend toward more symptoms showing significant improvement versus significant worsening of symptoms.

Extensive analyses were performed to evaluate the effect of both treatment (i.e., sphere only or spherocylindrical corrections) and of optical zone size on patient symptoms with the majority of patient symptoms remaining unchanged from baseline. More symptoms were described by patients as better or significantly better at both 3 and 6 months than were described as worse or significantly worse than at baseline, as shown in Table 15, below.

TABLE 15

COMPARISON OF SYMPTOMS BEFORE AND AFTER SURGERY ANALYZED BY OPTIC ZONE AT 6 MONTHS

Symptom	Significantly Better	Better	No Change	Worse	Significantly Worse
6 Months (N=73) Optical Zone Size 5.75 to 6.24					
Light Sensitivity	2.7%	19.2%	68.5%	6.8%	2.7%
Headache	0.0%	16.4%	79.5%	2.7%	1.4%
Pain	0.0%	2.7%	97.3%	0.0%	0.0%
Redness	2.7%	15.1%	76.7%	5.5%	0.0%
Dryness	0.0%	11.0%	47.9%	35.6%	5.5%
Excessive Tearing	0.0%	6.8%	87.7%	5.5%	0.0%
Burning	0.0%	5.5%	82.2%	12.3%	0.0%
Gritty Feeling	0.0%	2.7%	89.0%	8.2%	0.0%
Glare	1.4%	21.9%	61.6%	9.6%	5.5%
Halos†	0.0%	6.8%	78.1%	9.6%	5.5%
Blurring of Vision	11.0%	5.5%	61.6%	15.1%	6.8%
Double Vision	0.0%	0.0%	91.8%	1.4%	6.8%
Ghost Images**	0.0%	4.1%	91.8%	2.7%	1.4%
Fluctuation of Vision*	0.0%	5.6%	66.2%	21.1%	7.0%
Variation in Vision***					
In Bright Light	0.0%	15.1%	71.2%	13.7%	0.0%
In Normal Light	0.0%	6.8%	82.2%	8.2%	2.7%
In Dim Light	4.1%	16.4%	63.0%	15.1%	1.4%
Night Driving Difficulty	8.2%	34.2%	47.9%	6.8%	2.7%
6 Months (N=246) Optical Zone Size 6.25 to 6.74					
Light Sensitivity	11.4%	28.0%	52.8%	7.7%	0.0%
Headache	8.1%	19.9%	65.9%	4.9%	1.2%
Pain	3.3%	4.5%	89.4%	2.8%	0.0%
Redness	1.6%	22.0%	64.6%	11.0%	0.8%
Dryness	4.1%	19.5%	49.2%	25.6%	1.6%
Excessive Tearing	2.0%	11.4%	82.9%	2.8%	0.8%
Burning	1.6%	15.4%	75.6%	6.9%	0.4%
Gritty Feeling	0.8%	10.2%	83.7%	5.3%	0.0%
Glare	4.1%	15.9%	65.4%	11.8%	2.8%
Halos	2.0%	12.6%	69.9%	13.4%	2.0%
Blurring of Vision	8.1%	13.8%	58.9%	15.9%	3.3%
Double Vision	0.0%	1.2%	96.7%	0.8%	1.2%
Ghost Images**	0.0%	3.3%	91.8%	4.1%	0.8%
Fluctuation of Vision*	0.0%	7.0%	68.3%	21.0%	3.7%
Variation in Vision***					
In Bright Light	4.9%	21.6%	62.9%	10.2%	0.4%
In Normal Light	1.2%	8.2%	78.4%	9.8%	2.4%
In Dim Light	3.7%	22.4%	55.5%	15.1%	3.3%
Night Driving Difficulty	11.8%	26.8%	50.0%	10.6%	0.8%

TABLE 15 CONT'D

COMPARISON OF SYMPTOMS BEFORE AND AFTER SURGERY ANALYZED BY OPTIC ZONE AT 6 MONTHS

Symptom	Significantly Better	Better	No Change	Worse	Significantly Worse
6 Months (N=20) Optical Zone Size 6.75 to 7.24					
Light Sensitivity	5.0%	50.0%	45.0%	0.0%	0.0%
Headache	0.0%	25.0%	75.0%	0.0%	0.0%
Pain	0.0%	0.0%	100.0%	0.0%	0.0%
Redness	0.0%	40.0%	40.0%	10.0%	10.0%
Dryness	0.0%	0.0%	55.0%	45.0%	0.0%
Excessive Tearing	10.0%	5.0%	85.0%	0.0%	0.0%
Burning	0.0%	15.0%	85.0%	0.0%	0.0%
Gritty Feeling	0.0%	0.0%	90.0%	10.0%	0.0%
Glare	0.0%	20.0%	55.0%	25.0%	0.0%
Halos†	0.0%	20.0%	80.0%	0.0%	0.0%
Blurring of Vision	0.0%	45.0%	55.0%	0.0%	0.0%
Double Vision	0.0%	5.0%	95.0%	0.0%	0.0%
Ghost Images**	0.0%	15.0%	85.0%	0.0%	0.0%
Fluctuation of Vision*	0.0%	15.0%	80.0%	5.0%	0.0%
Variation in Vision***					
In Bright Light	0.0%	20.0%	80.0%	0.0%	0.0%
In Normal Light	0.0%	15.0%	85.0%	0.0%	0.0%
In Dim Light	20.0%	10.0%	60.0%	10.0%	0.0%
Night Driving Difficulty	10.0%	40.0%	50.0%	0.0%	0.0%

* Fluctuation in Vision only reported on for n=336 eyes at 3 months and 335 eyes at 6 months

** Ghost images was reported on for n=339 eyes at 6 months

*** Variation in Vision was reported on for only n=339 eyes at 6 months

4.2.9.4 Patient Subjective Evaluations

Presented in Table 16 are the results for the patient subjective assessments of their overall quality of vision after the surgery, whether or not they would choose to have the surgery again if given the choice, and their overall satisfaction with the surgery.

TABLE 16

SELF-EVALUATION OVERALL QUALITY OF VISION
ALL TREATED EYES

Overall Quality Of Vision After Excimer Laser?	VISITS		
	1 MONTH	3 MONTH	6 MONTH
Total Eyes Reported *	340	340	340
Not Reported **	0	0	0
Distribution Of Scores	% (n)	% (n)	% (n)
Extreme improvement	80.6 % (274)	81.8 % (278)	84.7 % (288)
Marked improvement	16.2 % (55)	14.1 % (48)	12.1 % (41)
Moderate improvement	2.4 % (8)	2.1 % (7)	1.8 % (6)
Slight improvement	0.9 % (3)	1.8 % (6)	1.2 % (4)
No improvement	0.0 % (0)	0.3 % (1)	0.3 % (1)

Choose Excimer Laser Again?	VISITS		
	1 MONTH	3 MONTH	6 MONTH
Total Eyes Reported *	337	338	340
Not Reported **	3	2	0
Distribution Of Scores	% (n)	% (n)	% (n)
Yes	97.0 % (327)	97.3 % (329)	98.2 % (334)
Unsure	3.0 % (10)	2.7 % (9)	1.2 % (4)
No	0.0 % (0)	0.0 % (0)	0.6 % (2)

How satisfied with the Excimer Laser Results?	VISITS		
	1 MONTH	3 MONTH	6 MONTH
Total Eyes Reported *	340	337	340
Not Reported **	0	3	0
Distribution Of Scores	% (n)	% (n)	% (n)
Very Satisfied	89.7 % (305)	91.1 % (307)	90.9 % (309)
Moderately Satisfied	8.8 % (30)	7.1 % (24)	7.9 % (27)
Neutral	0.9 % (3)	1.8 % (6)	1.2 % (4)
Dissatisfied	0.6 % (2)	0.0 % (0)	0.0 % (0)
Very Dissatisfied	0.0% (0)	0.0 % (0)	0.0 % (0)

* Number of CRFs received with non-missing values at each visit.
** Number of CRFs received with missing values at each visit.

4.2.10 RETREATMENT

No data is available for LASIK retreatment using the Zyoptix system.

4.2.11 COMPARISON TO CONVENTIONAL LASIK (BASED ON MANIFEST PHOROPTER REFRACTION)

A clinical trial was conducted in 40 patients who underwent conventional LASIK in one eye and Zyoptix LASIK in the other eye, to allow a comparison of the two procedures.

4.2.11.1 Changes in Amount of Higher Order Aberration Postoperative

In the contralateral study of 40 patients, the average increase in Higher Order Aberrations over a 6.0 mm Wavefront analysis diameter was evaluated. The amount of postoperative higher-order aberrations was less for Zyoptix LASIK eyes than for the Conventional LASIK eyes. The average increase in higher-order aberrations after surgery was:

- +13.4% at 6 months for Zyoptix LASIK eyes.
- +45.3% at 6 months for Conventional LASIK eyes.

Eyes with greater preoperative Higher Order Aberrations (HOA) were more likely to have a reduction in HOA or less of an increase 6 months after surgery.

When evaluated as a function of the optic zone size used, the results indicated that Higher Order Aberration increases were less in eyes treated with larger optical zones.

4.2.11.2 Proportion of the Population with a Decrease in Higher Order Aberrations Postoperative

For most patients, the Zyoptix LASIK did not reduce Higher Order Aberrations from baseline. In the contralateral study of 40 patients, the proportion of the population with reduced Higher Order Aberrations over the 6.0mm wavefront analysis diameter after surgery compared to before surgery is found below:

- 37.5% at 6 months for Zyoptix LASIK eyes.
- 12.8% at 6 months for Conventional LASIK eyes.

For the 40 patients in the study who received Zyoptix LASIK in one eye and Conventional LASIK in the other eye, there was no significant difference in subjective symptoms between the two treatments.

The analysis of the Higher Order Aberrations present preoperative and postoperative confirms that the Zyoptix LASIK procedure shows improvements to be primarily in 3rd order aberrations (coma and trefoil). The impact on reducing Higher Order Aberrations is directly correlated to the magnitude of the specific Order of Aberration present prior to treatment.

TABLE 17A

CHANGE FROM BASELINE IN WAVEFRONT ABERRATION RMS AT 6 MONTH VISIT AS A FUNCTION OF PREOPERATIVE HIGHER ORDER WAVEFRONT ABERRATION MAGNITUDE

6.0 MM WAVEFRONT ANALYSIS DIAMETER

	Preoperative Higher Order Root Mean Square (RMS)									
	0.00-0.24um		**0.25-0.49um**		**0.50-0.74um**		**0.75-0.99um**		**1.00-1.24um**	
N	**47**		**200**		**78**		**9**		**2**	
Induced Aberration	um	%	um	%	um	%	um	%	um	%
Total RMS	-3.46	-81 ⇓	-3.90	-80 ⇓	-4.21	-78 ⇓	-4.84	-79 ⇓	-5.23	-78 ⇓
Higher Order	0.21	99 ⇑	0.16	44 ⇑	0.05	8 ⇑	-0.09	-11 ⇓	-0.28	-25 ⇓
2nd Order	-3.59	-84 ⇓	-4.08	-84 ⇓	-4.42	-83 ⇓	-5.08	-83 ⇓	-5.43	-82 ⇓
3rd Order	0.12	81 ⇑	0.07	26 ⇑	-0.08	-16 ⇓	-0.26	-37 ⇓	-0.41	-40 ⇓
4th Order	0.17	140 ⇑	0.16	71 ⇑	0.16	53 ⇑	0.13	31 ⇑	0.10	21 ⇑
5th Order	0.01	14 ⇑	0.02	25 ⇑	0.02	31 ⇑	0.02	24 ⇑	0.01	5 ⇑

TABLE 17B

CHANGE FROM BASELINE IN WAVEFRONT ABERRATION RMS AT 6 MONTH VISIT AS A FUNCTION OF OPTIC ZONE SIZE
6.0MM WAVEFRONT ANALYSIS DIAMETER

	Optic Zone Size					
	5.75-6.24mm		6.25-6.74mm		6.75-7.00mm	
n	73		242		20	
Induced Aberration	um	%	um	%	um	%
Total RMS	-4.82	-81 ⇓	-3.72	-79 ⇓	-3.23	-76 ⇓
Higher Order	0.20	43 ⇑	0.12	29 ⇑	0.07	17 ⇑
2nd Order	-5.08	-87 ⇓	-3.88	-83 ⇓	-3.34	-79 ⇓
3rd Order	0.06	16 ⇑	0.03	10 ⇑	-0.04	-12 ⇓
4th Order	0.23	92 ⇑	0.14	60 ⇑	0.14	78 ⇑
5th Order	0.02	34 ⇑	0.02	24 ⇑	0.01	21 ⇑

4.2.11.3 Comparative Results for Wavefront-Guided LASIK vs. Conventional LASIK

Table 18 compares the change in total wavefront error and in higher-order aberrations for spherical myopic eyes treated with Wavefront-guided LASIK and Conventional LASIK with the Zyoptix System manifest refraction in the Subgroup Study with matched conventional and Zyoptix treatments (N=40 patients). On a percentage basis, the reduction in total wavefront RMS error is essentially equivalent between the treatment types. On third order aberrations (coma) the Zyoptix LASIK results in a reduction of 16% whereas the Conventional LASIK causes an increase of 30%.

TABLE 18

CHANGE FROM BASELINE IN WAVEFRONT ABERRATION RMS AT 6 MONTH VISIT FOR MATCHED CONVENTIONAL AND ZYOPTIX EYES 6.0MM WAVEFRONT ANALYSIS DIAMETER

	Zyoptix		Conventional	
n	40		39	
Induced Aberration	um	%	um	%
Total RMS	-3.51	-81 ⇓	-3.40	-78 ⇓
Higher Order	0.06	14 ⇑	0.17	45 ⇑
2nd Order	-3.67	-85 ⇓	-3.59	-82 ⇓
3rd Order	-0.05	-16 ⇓	0.09	30 ⇑
4th Order	0.14	70 ⇑	0.17	84 ⇑
5th Order	0.02	28 ⇑	0.00	1 ⇑